Pathway Analysis of Integrin Alpha X/Beta 2 (CD11c/CD18) in the Murine Mononuclear Phagocyte Lineage

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Introduction:

Integrin alpha X (CD11c) is commonly used to discriminate dendritic cells from macrophages within the murine mononuclear phagocyte lineage. ITGAL (CD11a), ITGAM (CD11b), ITGAX and ITGAD (CD11d) all dimerise with the integrin beta2 subunit (CD18) and act as pattern recognition receptors. As a group these integrins mediate cellular adhesion, phagocytosis and co-stimulatory functions within MNPs; however specific functions following ITGAX binding have yet to be defined. In order to rationalise the available data and information on ITGAX and its potential functional role, we have attempted to construct a pathway diagram of integrin alpha/beta2-mediated signalling utilising the modified Edinburgh Pathway Notation (mEPN) scheme.

Methods:

Following the meta-analysis of lineage-specific gene expression signatures in mouse leukocyte populations[1], the profile of ITGAX mRNA was observed to co-cluster with a restricted set of genes (highlighted in purple), the products of which suggest novel functions involved in the regulation of the actin cytoskeleton. Extensive mining of the literature guided by protein interaction data available in the STRING (functional protein interaction networks) and REACTOME (a curated knowledgebase of biological pathways) databases was performed until specific interactions with cluster gene products were identified.

[1] Mabbott, *et al*., Immunobiology. 2010;215(9-10):724-36

Results:

Presented here is the current working pathway which operates as a detailed and extendable visual aid to understanding the functional context of ITGAX and this will be used to generate hypotheses and make *in silico* predictions of function.

Modified Edinburgh Pathway Notation (mEPN) Pallette

COMPONENT
- PROTEIN COMPLEX
- PEPTIDE, PROTEIN
- GENERIC ENTITY
- ION/SIMPLE MOLECULE
- SIMPLE BIOCHEMICAL
- DRUG

OTHER
- ENERGY/ MOLECLUAR TRANSFER
- PATHWAY OUTPUT

BOOLEAN LOGIC OPERATORS
- AND
- OR

PROCESS NODES
- BINDING
- CLEAVAGE
- DISSOCIATION
- CATALYSIS
- TRANSLOCATION
- ACTIVATION
- PHOSPHORYLATION
- AUTO-PHOSPHORYLATION
- OLIGOMERIZATION
- AUTO-CLEAVAGE
- RATE LIMITING CATALYSIS
- AUTO-CATALYSIS
- TRANSCRIPTION/TRANSLATION
- INHIBITION
- DEPHOSPHORYLATION
- SINK (PROTEASOMAL DEGRADATION)

EDGE ANNOTATION
- CATALYSES
- ACTIVATES
- INHIBITS
- INTERACTION
- DETAILS UNKNOWN
- TRANSLOCATION
- PROPOSED NOVEL ASSOCIATIONS

CELLULAR COMPARTMENTS
- CELL MEMBRANE
- CYTOPLASM
- NUCLEUS
- LYSOSOME

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Resources:
1. The macrophage community website: http://www.macrophages.com/
2. mEPN: http://www.mepn-pathway.org/
3. String: http://string-db.org/
4. Reactome: http://www.reactome.org/